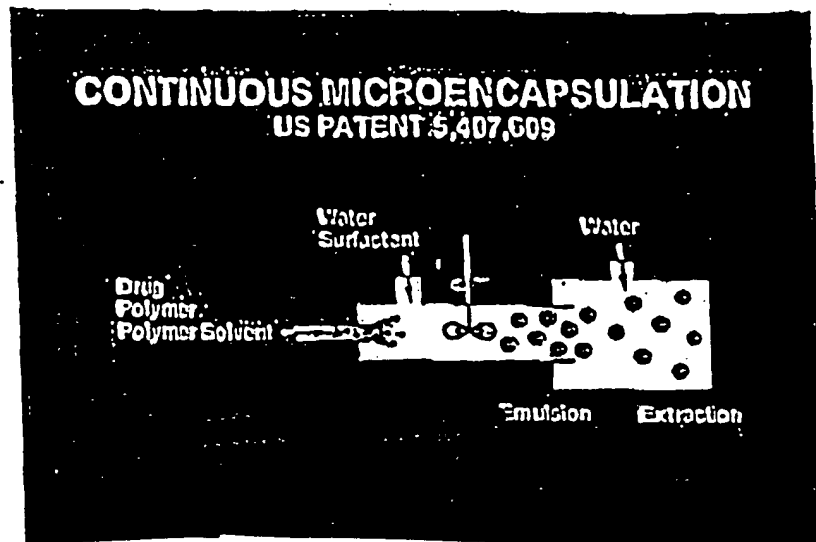




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## SOUTHERN RESEARCH'S PATENTED MICROENCAPSULATION PROCESS



### Advantages

- US Patent issued 1995
- Fast encapsulation time -- milliseconds
- Minimal exposure to polymer solvent
- High encapsulation efficiency
- Good Yields
- Makes small microparticles  
    <100 micron <10 micron

### Drugs Microencapsulated

- Proteins
- Peptides
- Small molecules
- Water-soluble drugs
- Hydrophobic drugs
- Drugs encapsulated in  
    lactide/glycolide polymers

FIGURE 1

FIGURE 2

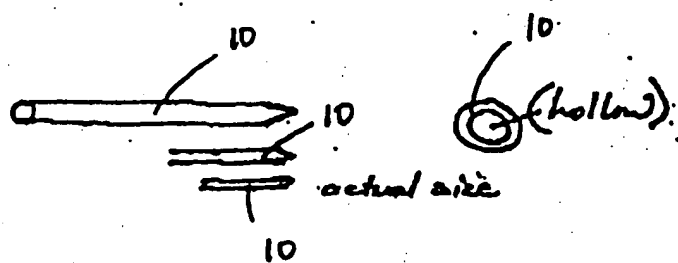
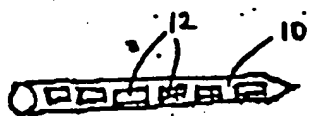
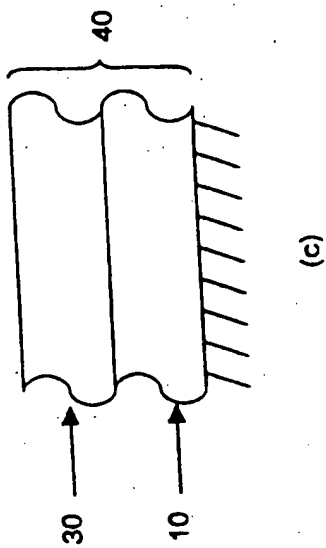
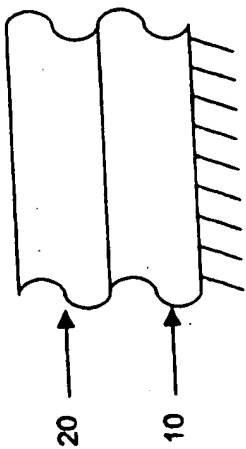


FIGURE 3

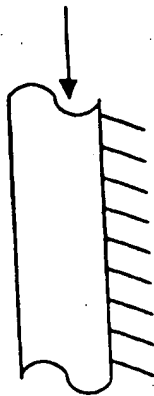




(c)



(b)



(a)

FIGURE 4

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Hardness:	F	B	3B	4B	F

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Hardness:	F	B	9B	<9B	F

Hardness Rating:

2H-H-F-HB-B-2B-3B-4B-5B-6B-7B-8B-9B  
 Harder ← → Softer

FIGURE 5

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Resistance To Cracking	< 3 mm	< 3 mm	< 3mm	< 3mm	<3mm

Conditions: 5 minutes in 37°C pH 7.4 Saline Buffer

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Resistance To Cracking	< 3 mm	< 3 mm	< 3mm	< 3mm	< 3mm

FIGURE 6

Conditions: Ambient

Material:	PX510	PX261	PX749	PX125	PX510 + 14% Paclitaxel
Class:	5B	5B	5B	4B	5B

Class Rating: 5B = 0% of coating removed from substrate  
 4B = Less than 5% of coating removed from substrate

FIGURE 7

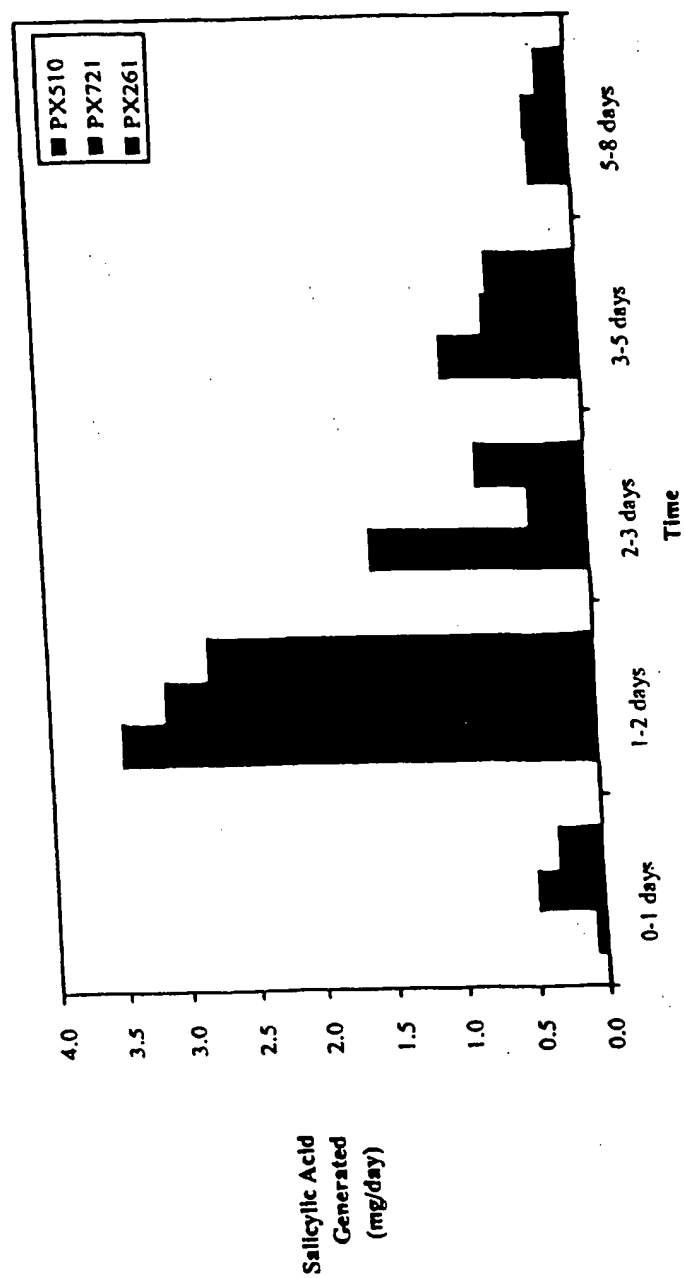


FIGURE 8

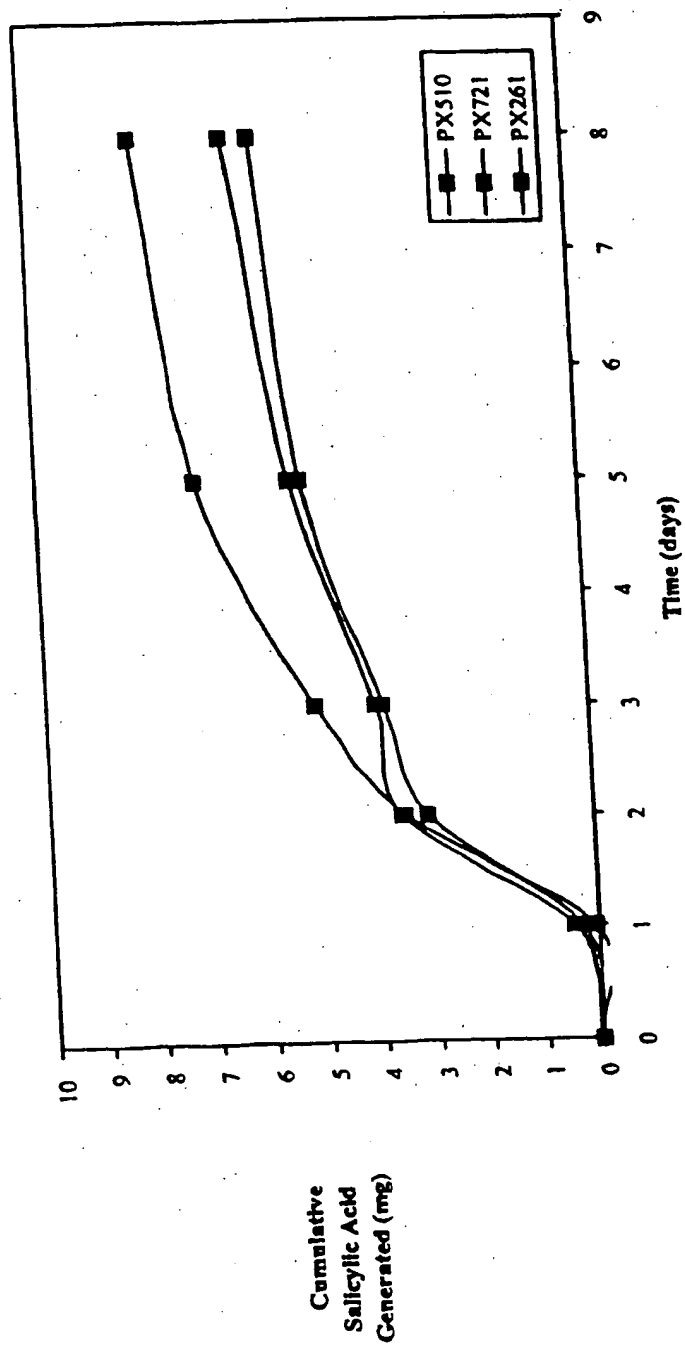


FIGURE 8B



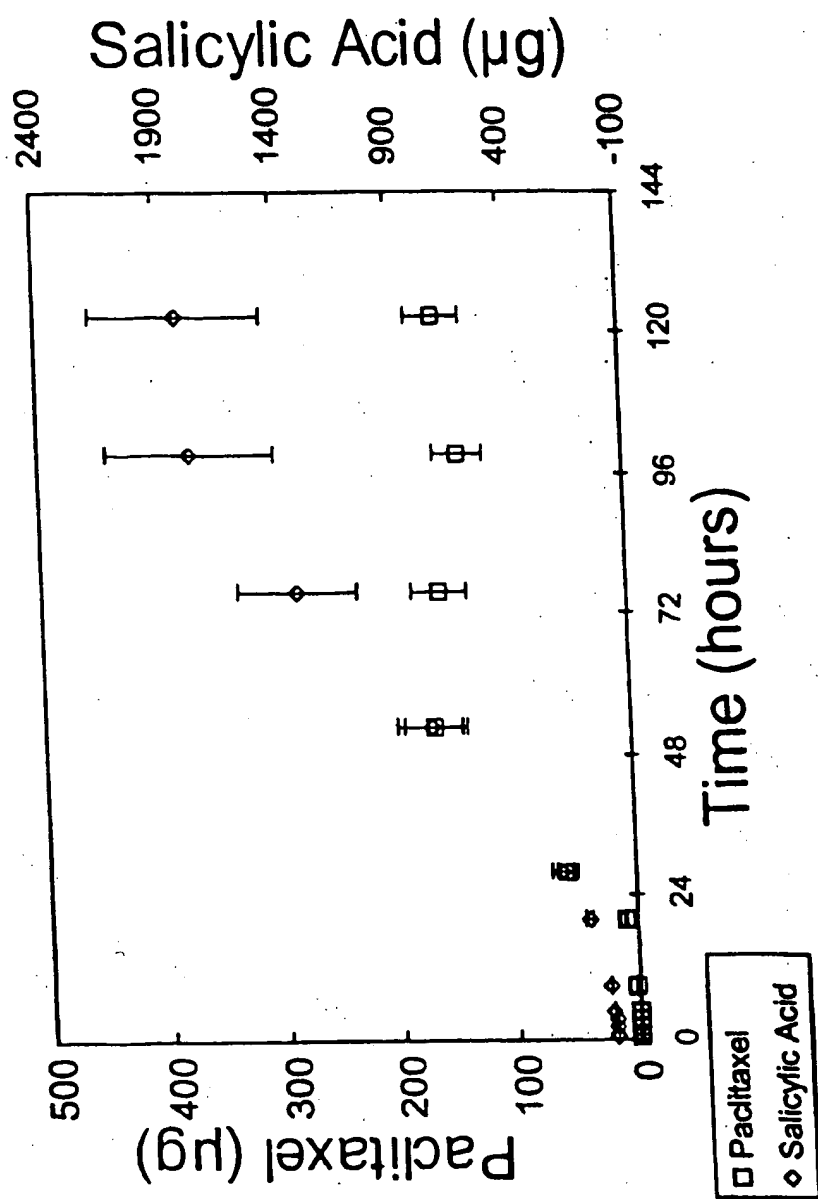
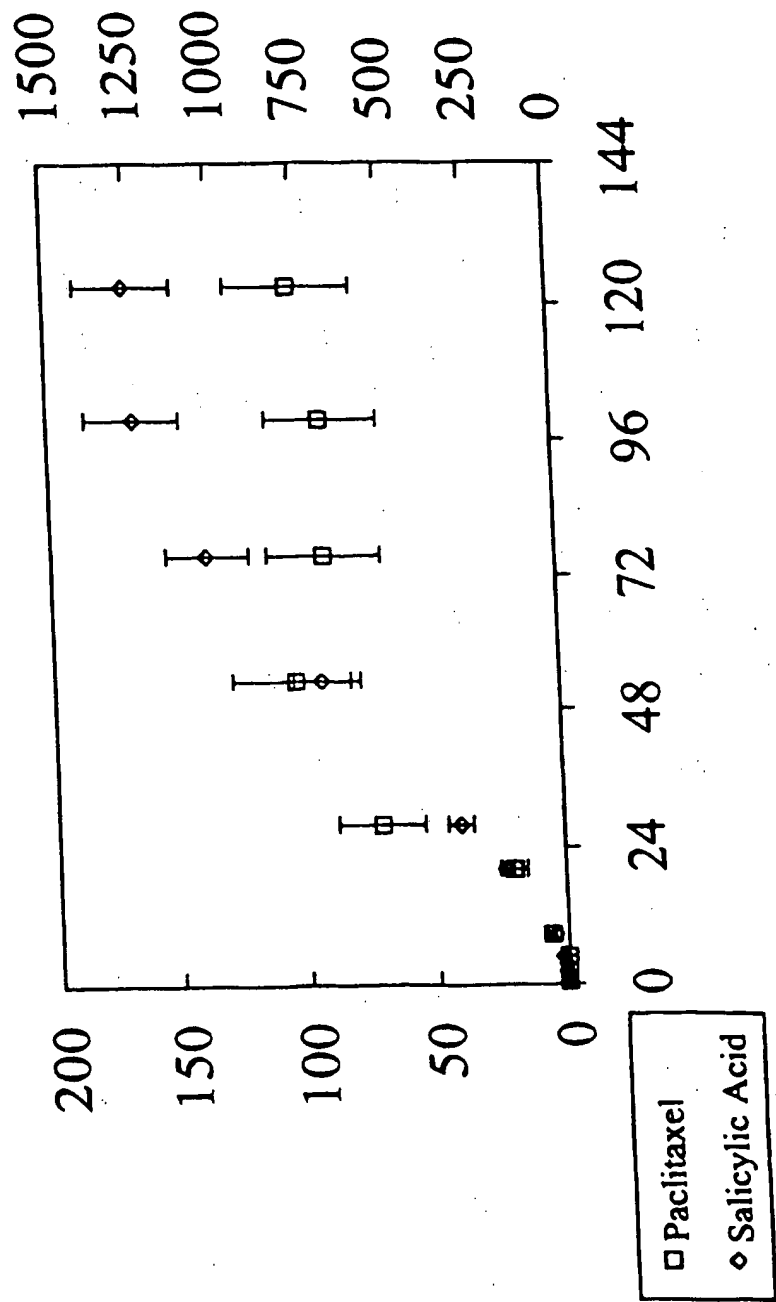


FIGURE 9A



**FIGURE 9B**

Property	Formulation			
	PX510	PX721	PX261	PX749
$T_g$ ( C )	44	38	29	16
Tensile modulus (MPa)	2.0 (25 C) 5.1 (37 C)			3.0 (25 C)
Yield Strength (MPa)	Not observed			6.0 (25 C)
Ultimate Elongation (%)	1.5 (25 C) 350 (37 C)			500 (25 C)

FIGURE 10

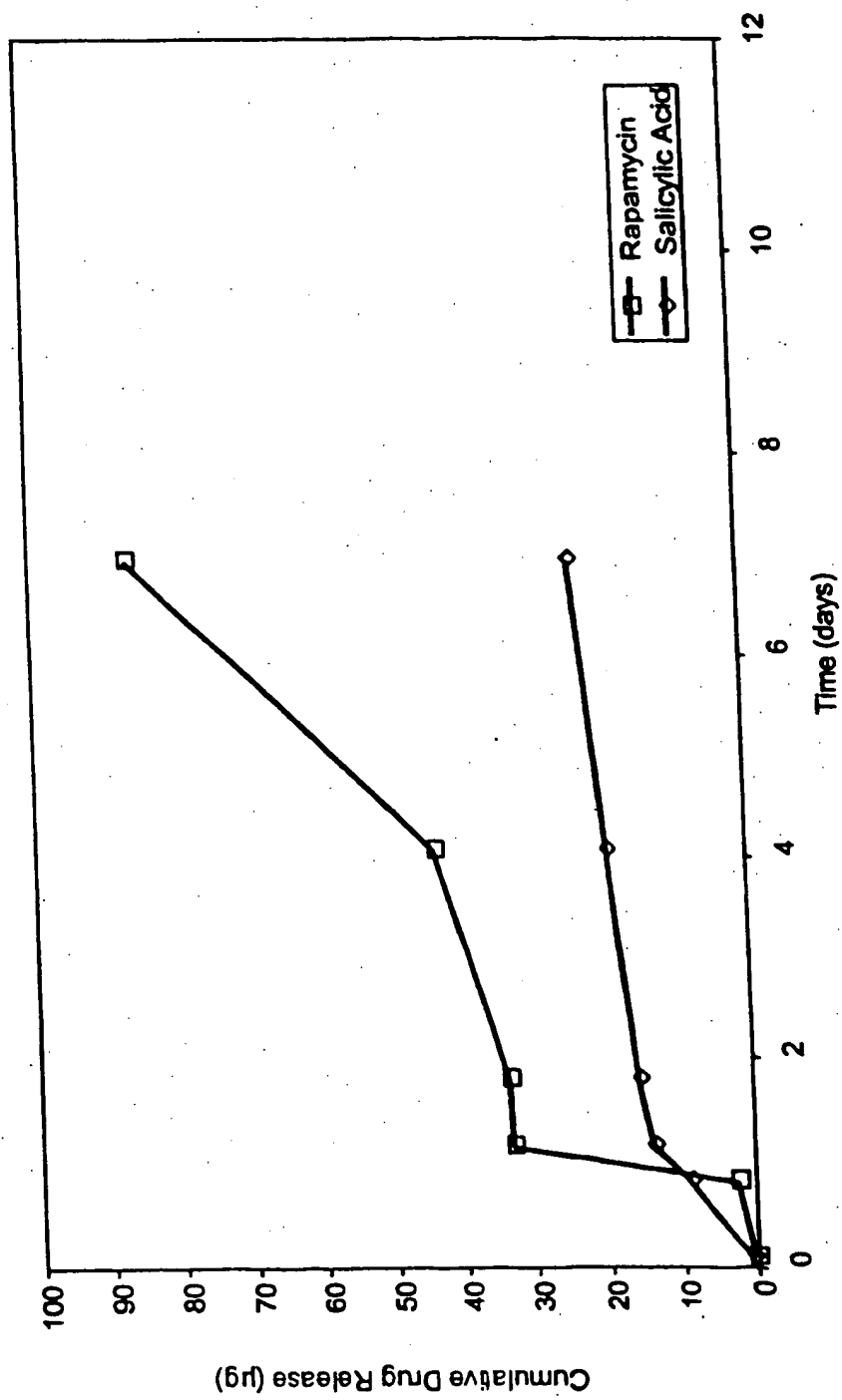


FIGURE 11

E Beam (3 MRad)		$\gamma$ (25-35 KGys)			
Property	PX510	PX721	PX261	PX510	PX721 PX261
MW	-28%	-39%	-26%	-14%	N/C N/C
Hardness	-2 units	N/C	-1 unit	N/C	-3 units -2 units
Flexibility	N/C	N/C	N/C	N/C	N/C N/C
Adhesion	N/C	N/C	-1 unit	N/C	N/C N/C

N/C: no change

FIGURE 12

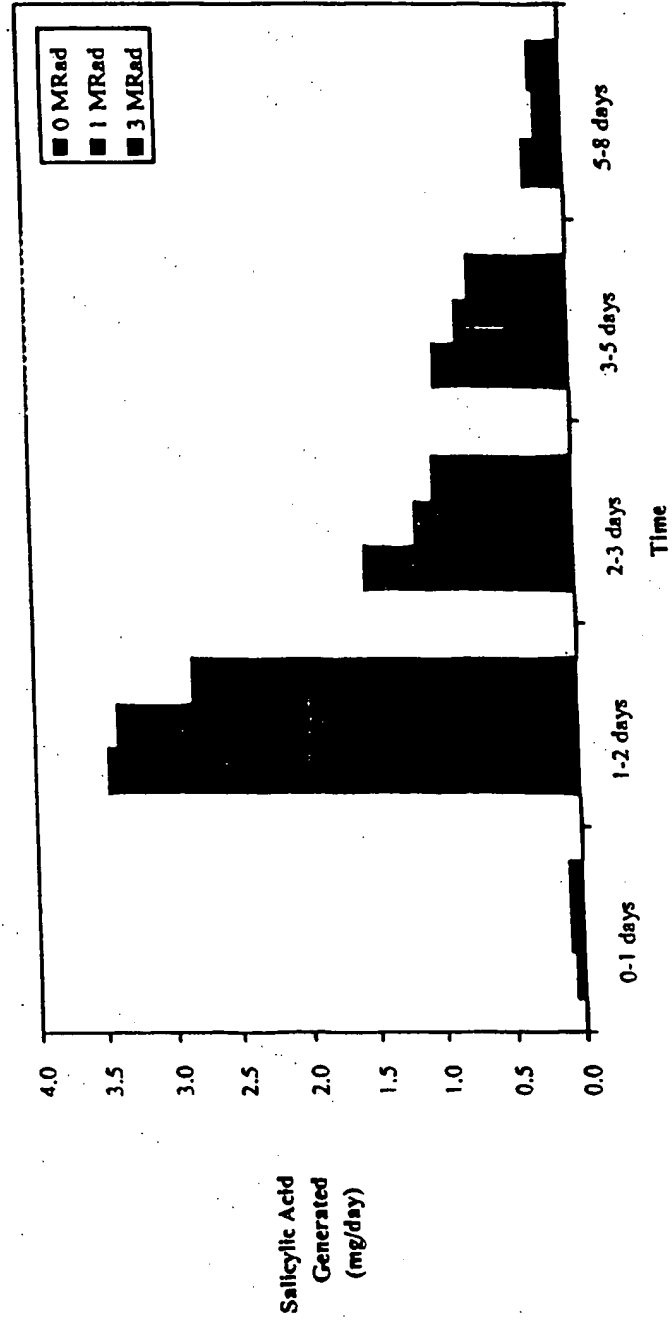


FIGURE 13A

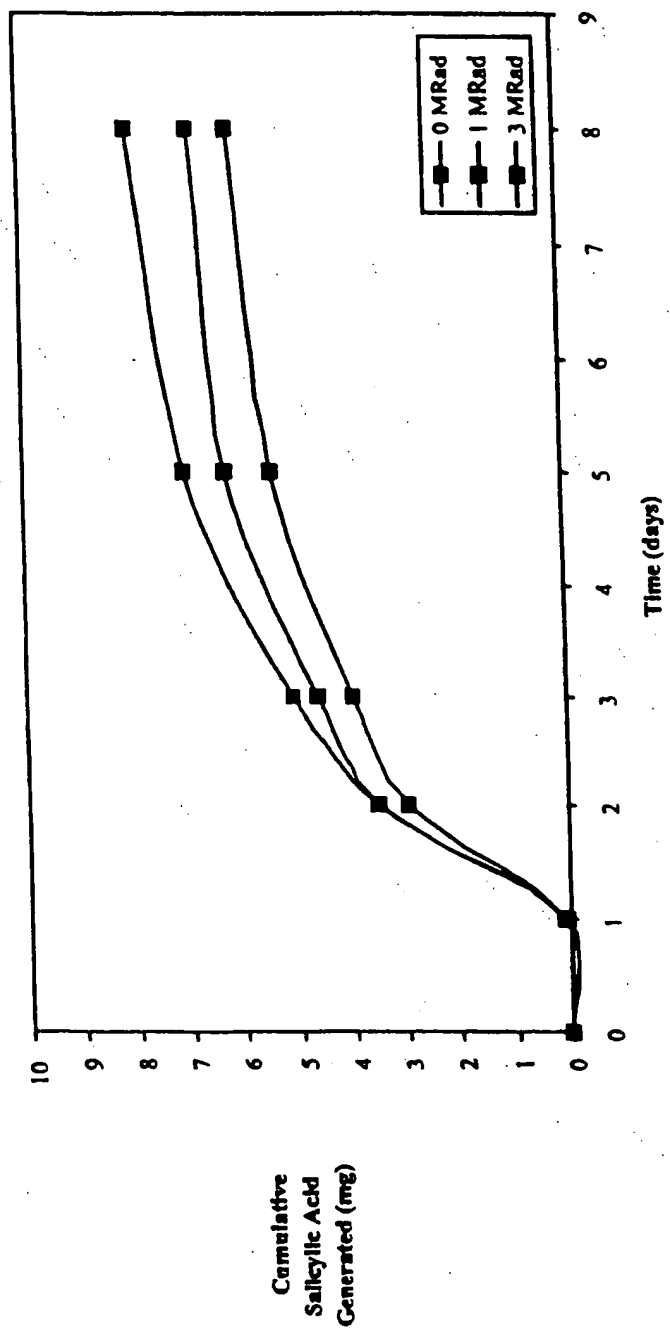


FIGURE 13B

# PX242 20-53 Coated Coupon Diflunisal Elution

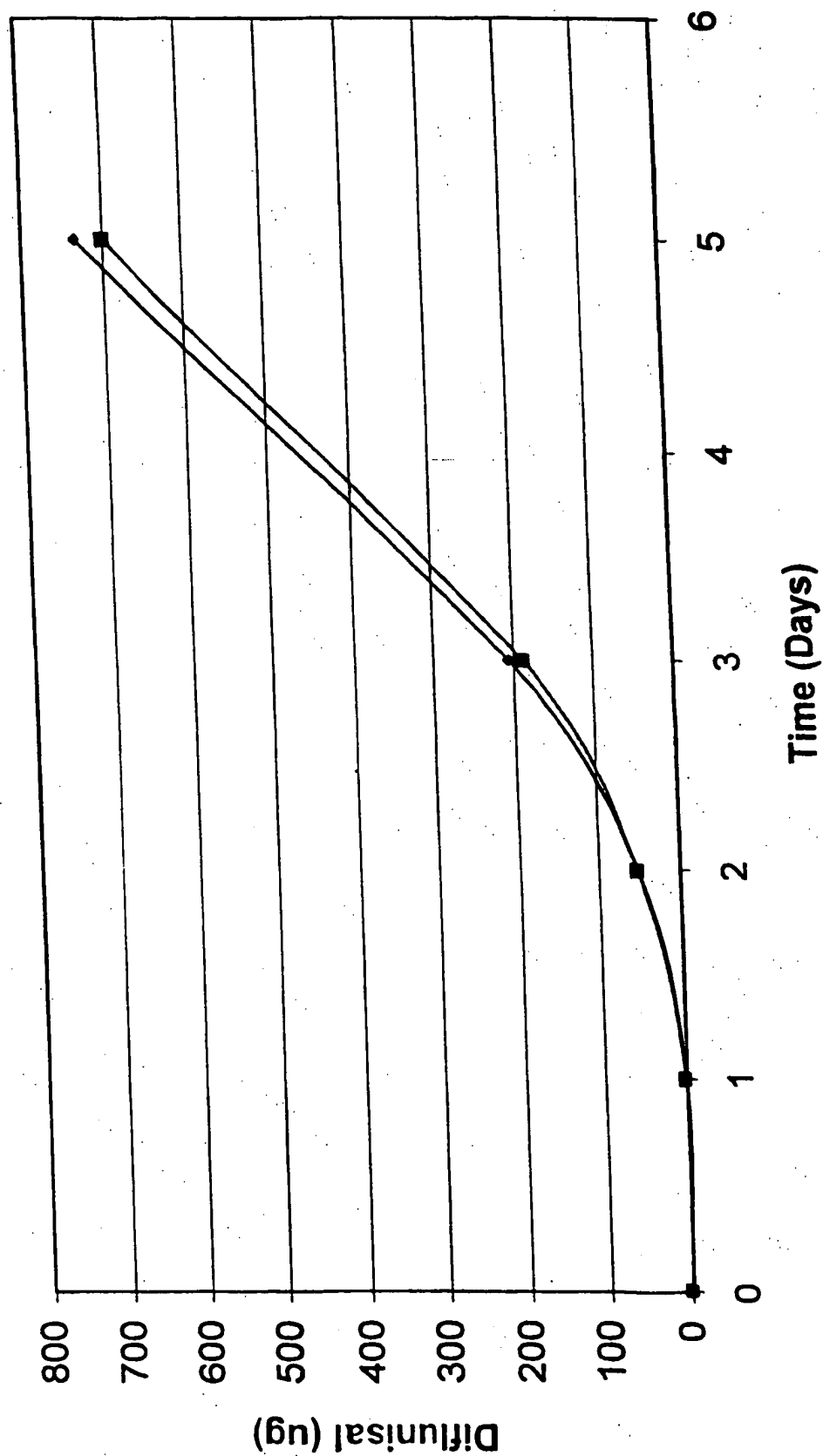


FIGURE 14



# PX242 20-53 Coated Coupon Diflunisal Elution

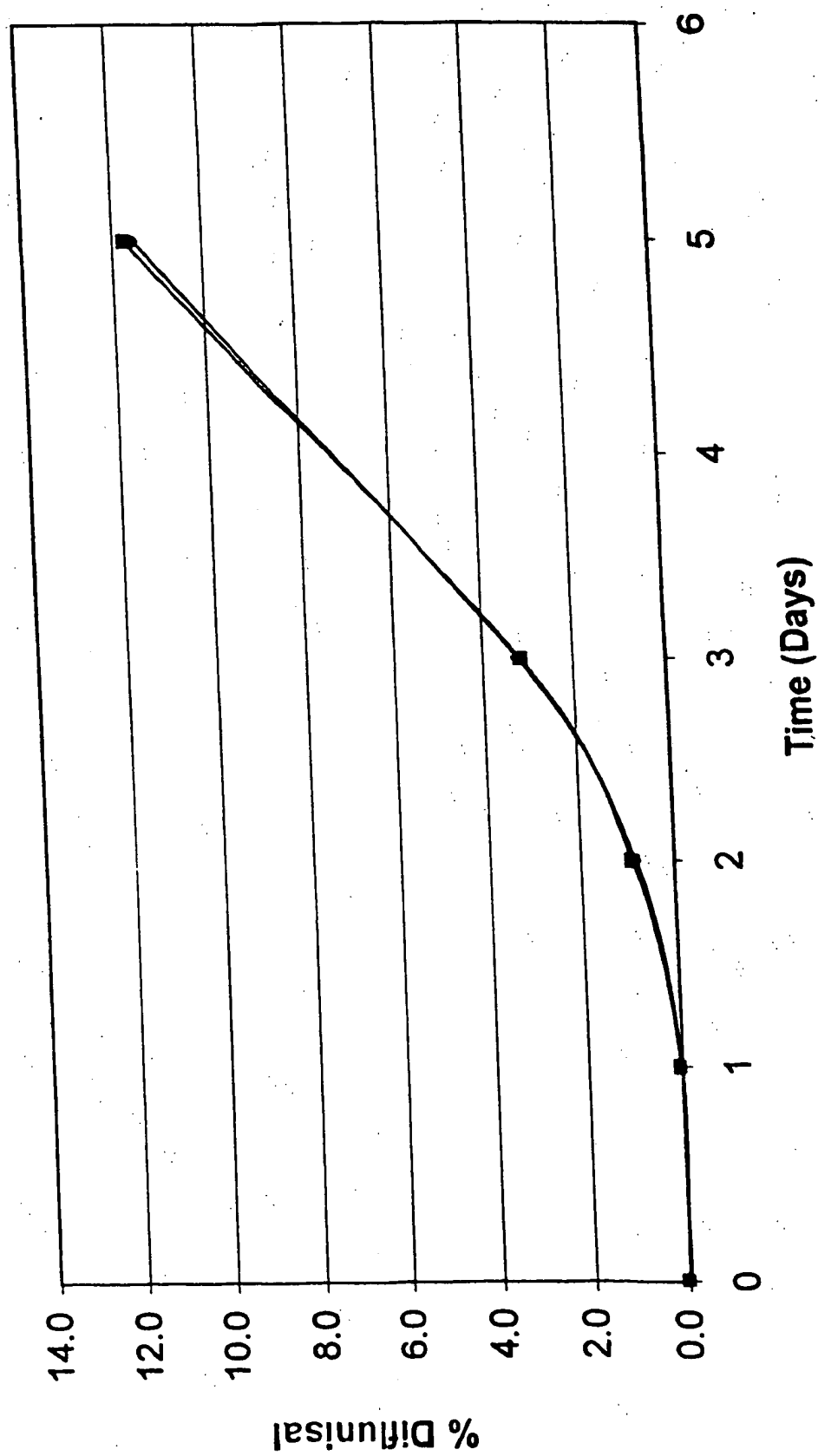
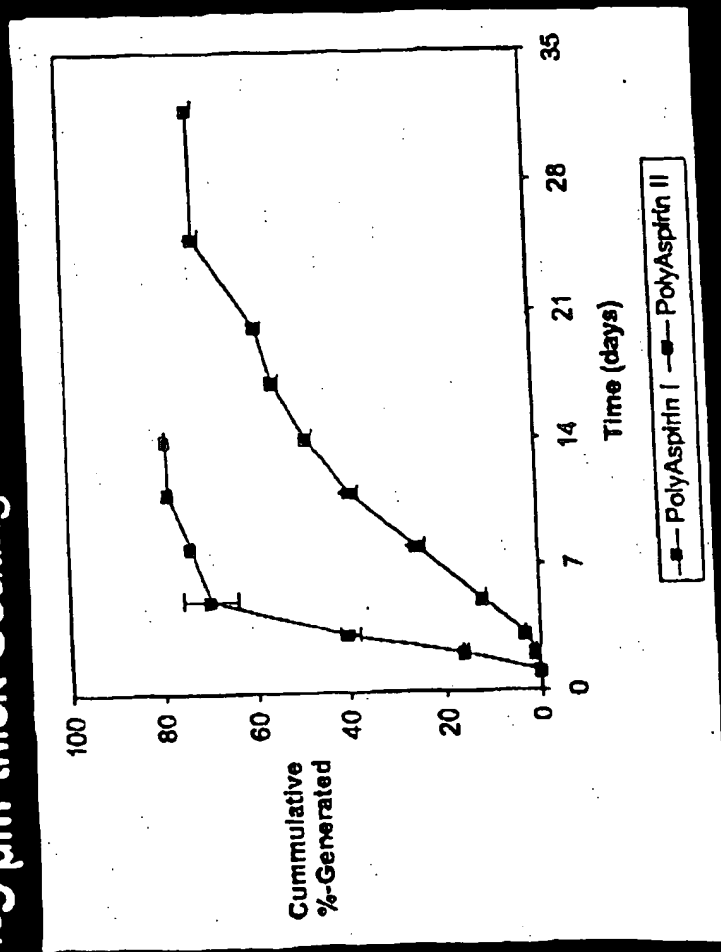


FIGURE 15

# Erosion of PolyAspirin I & II

Generation of NSAID into 37 °C pH 7.4 PBS from  
~5  $\mu$ m-thick Coatings on 316L SS Plates



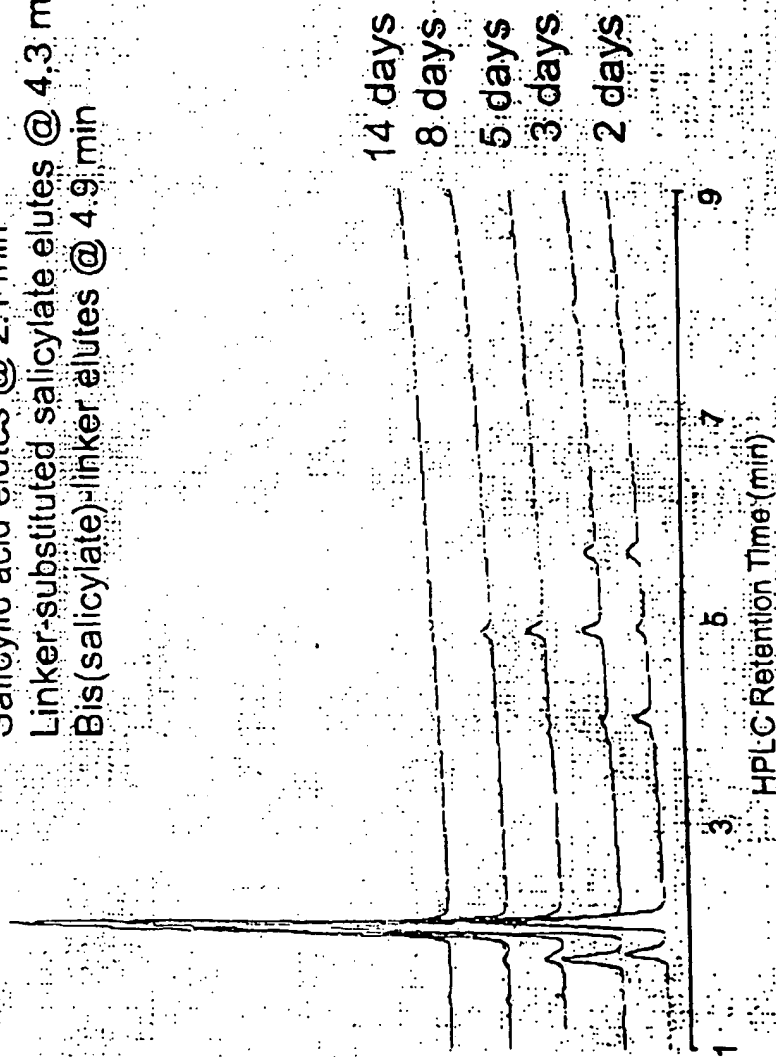
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FIGURE 16

# Erosion Profile for PolyAspirin I

Salicylic acid elutes @ 2.1 min  
Linker-substituted salicylate elutes @ 4.3 min  
Bis(salicylate)-linker elutes @ 4.9 min

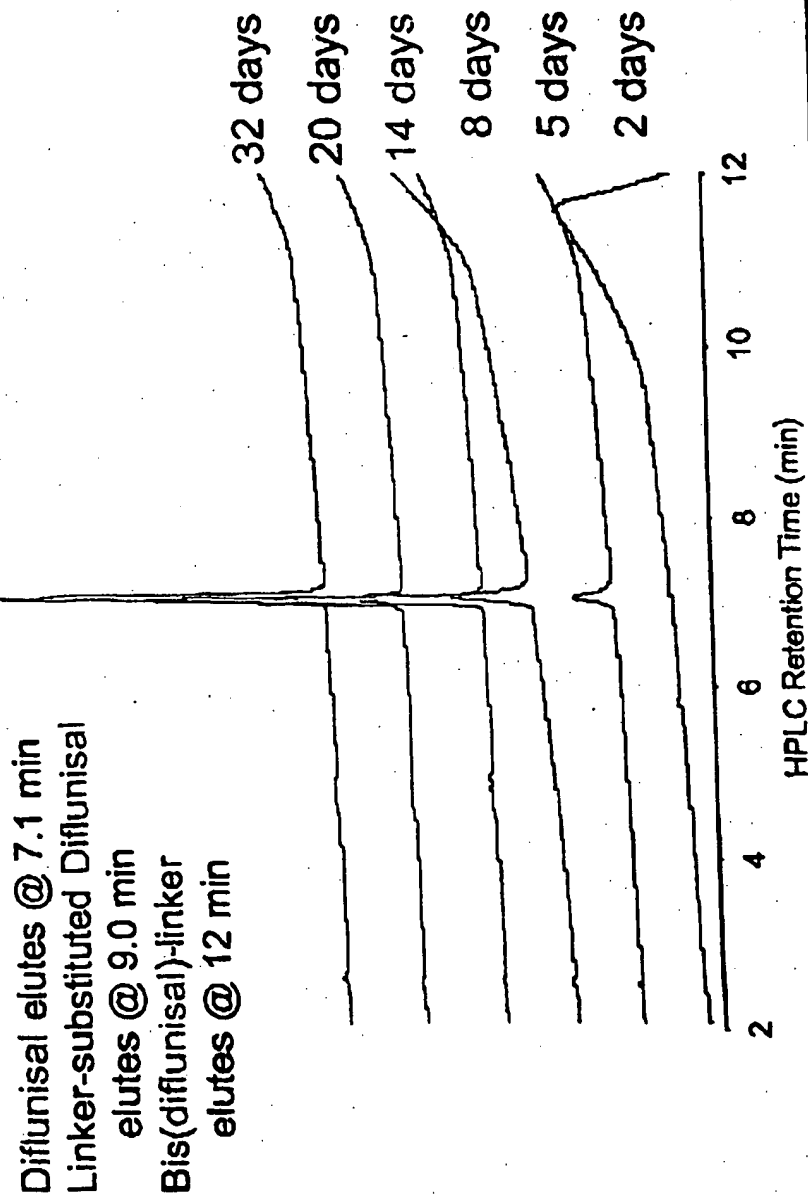


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FIGURE 17

# Erosion Profile for PolyAspirin II



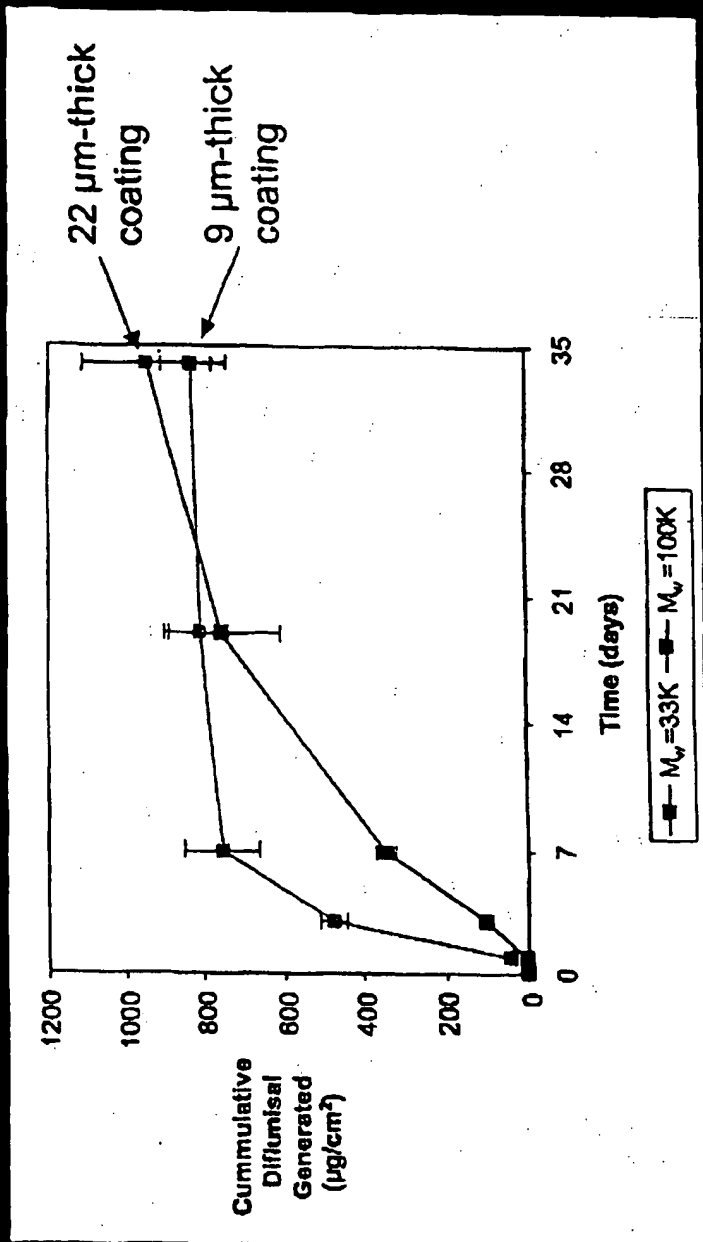
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FIGURE 18

# Effect of MW on Erosion

Generation of Diflunisal from PolyAspirin II into  
37 °C Serum from Coatings on 316L SS Plates

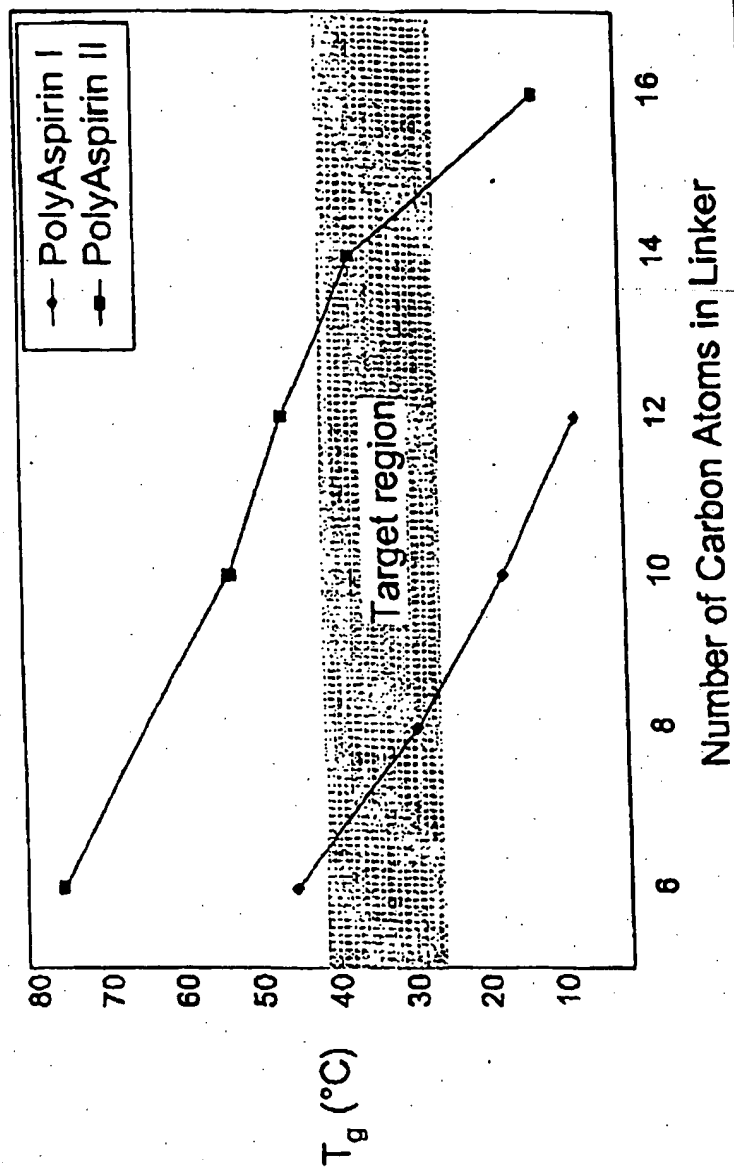


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FIGURE 19

# Tuning Mechanical Properties



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FIGURE 20

# Thermoanalysis of PolyAspirin™

## PolyAspirin I      PolyAspirin II

Property	PX261	PX857
	$M_w \sim 20K$	$M_w \sim 33K$
		$M_w \sim 100K$

$T_g$ (°C)	29	36	44
Ultimate Stress (kPa)	1700 (25°C) >2000 (37°C)	>2800 (25°C)	>2600 (25°C)
Ultimate Elongation (%)	>500 (25°C) >500 (37°C)	>4 (25°C)	>500 (25°C)
Toughness (kPa)	>3900 (25°C) >4400 (37°C)	>560 (25°C)	>4000 (25°C)

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FIGURE 21

# Properties of PolyAspirin™ Coatings

## PolyAspirin I      PolyAspirin II

PX281      PX657  
 $M_w \sim 20K$        $M_w \sim 33K$        $M_w \sim 100K$

### Test

#### Hardness

Ambient

5 min in PBS, 37 °C

1 hr in PBS, 37 °C

F      3H  
 2B      B  
 8B      4B

#### Flexibility

Ambient

5 min in PBS, 37 °C

1 hr in PBS, 37 °C

<3 mm      <3 mm  
 <3 mm      <3 mm  
 <3 mm      <3 mm

#### Adhesion

Ambient

5B      5B

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FIGURE 22



# PolyAspirin Coatings with Admixtures

## PolyAspirin II (PX657)

No Admixture      20% Pacitaxel Admixed

Test

### Hardness

Ambient

5 min in PBS, 37 °C

1 hr in PBS, 37 °C

F

F

6B

F

2B

8B

### Flexibility

Ambient

5 min in PBS, 37 °C

1 hr in PBS, 37 °C

<3 mm

<3 mm

<3 mm

<3 mm

<3 mm

<3 mm

### Adhesion

Ambient

5B

5B

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FIGURE 23

# Erosion of PolyAspirin I & II

## Diffunisal Generation & Pacitaxel Release into 37 °C Serum from ~5 µm-thick Coatings on 316L SS Plates

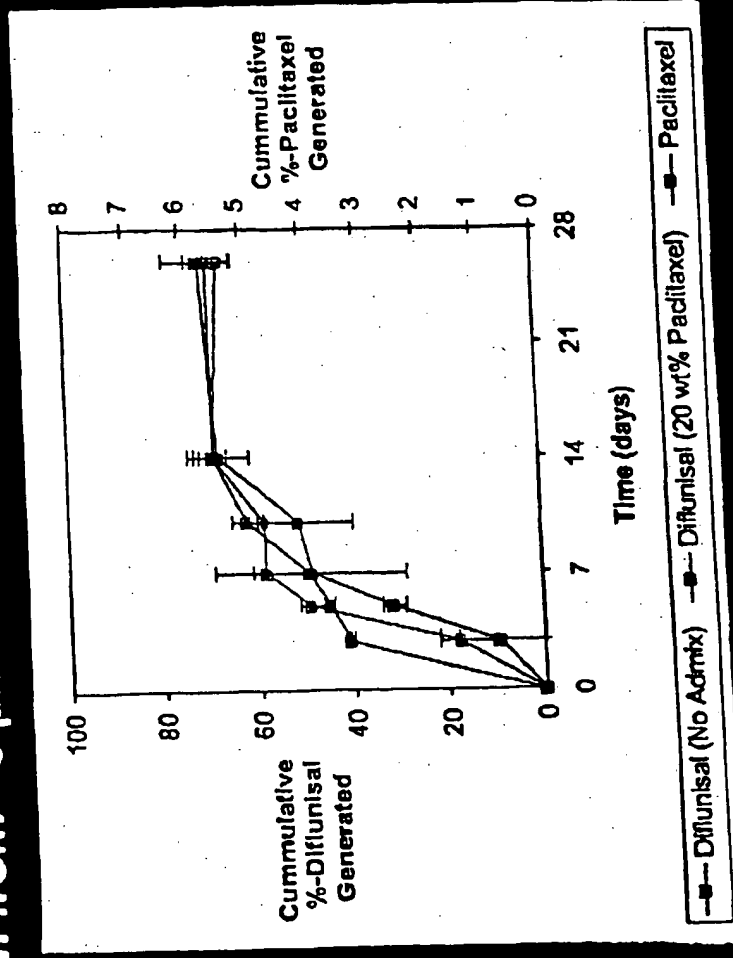


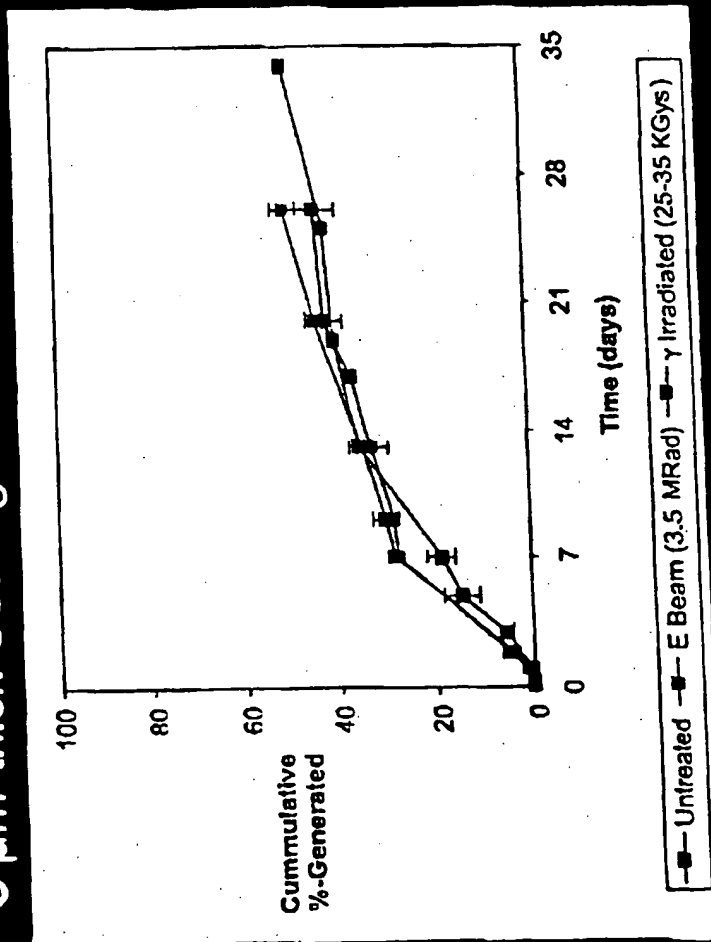
FIGURE 24

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# Erosion of Sterilized PolyAspirin II

Generation of Diflunisal into 37 °C Serum from  
~5 µm-thick Coatings on 316L SS Plates



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FIGURE 25

# $\gamma$ Irradiation (25-35 Kgys)

PolyAspirin I

PolyAspirin II

PX281

PX857

$M_w \sim 20K$

$M_w \sim 100K$

Property

MW

N/C

-50%

Hardness

-2 units

-3 units

Flexibility

N/C

.

Adhesion

N/C

.

N/C: no change

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FIGURE 26

# E Beam (3-4.5 MRad)

## PolyAspirin I      PolyAspirin II

PX261	PX657
$M_w \sim 20 K$	$M_w \sim 33K$ $M_w \sim 80K$

Property

MW

-26%

+5%

-30%

Hardness

-1 unit

+2 units

N/C

Flexibility

N/C

.

N/C

Adhesion

-1 unit

.

.

N/C: no change

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FIGURE 27

# Kinetics of NSAID Generation

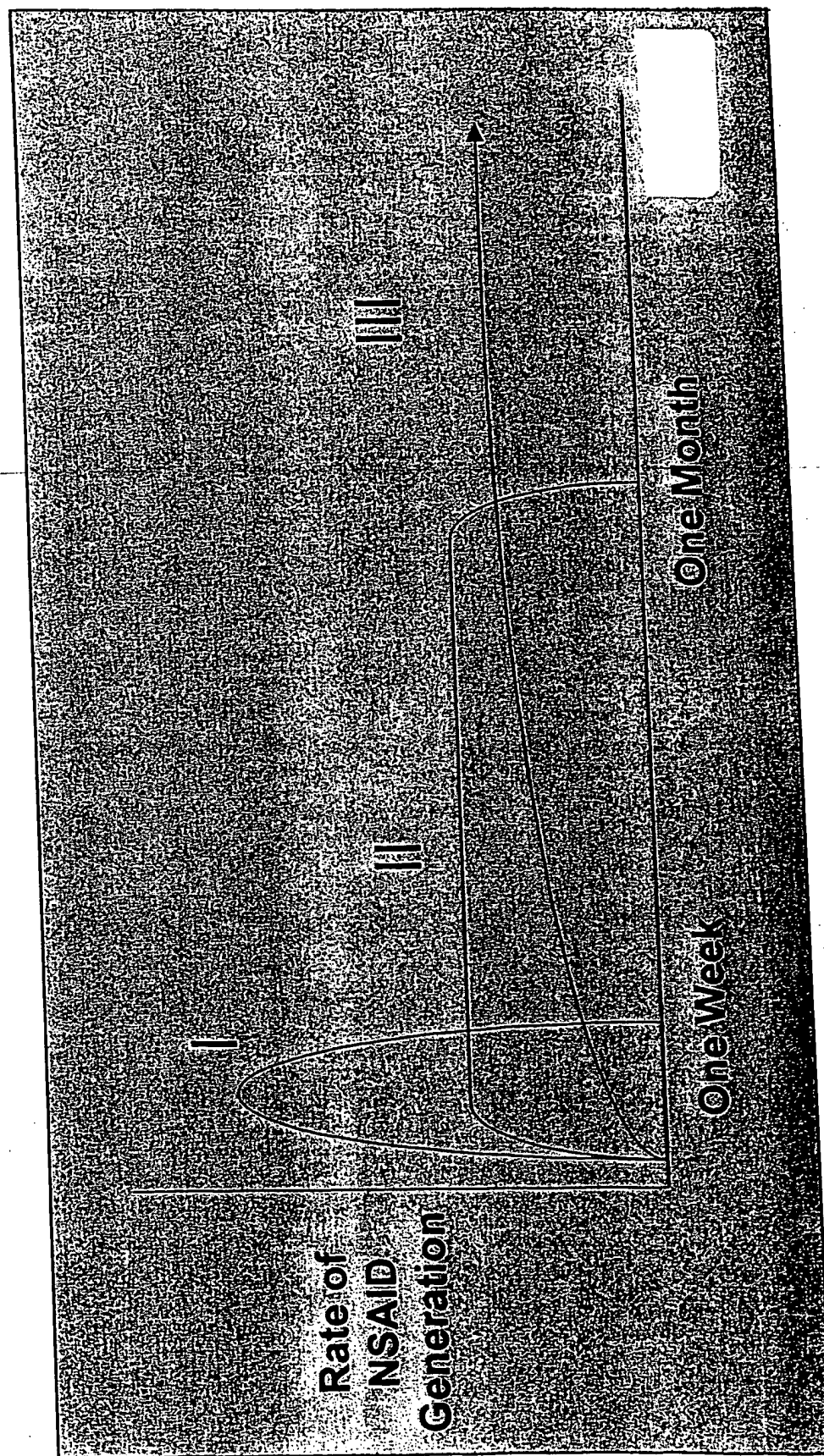
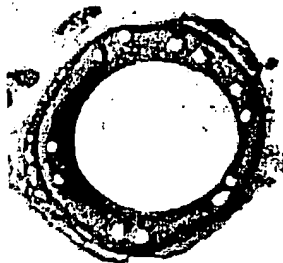
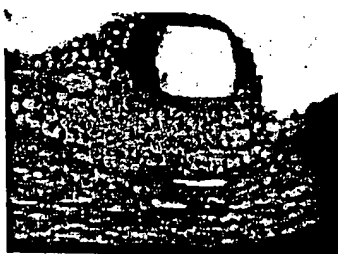


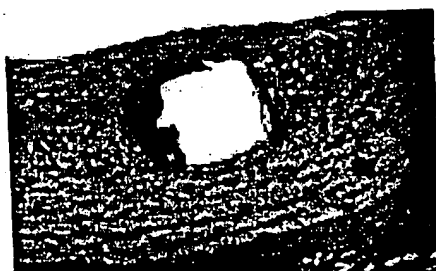
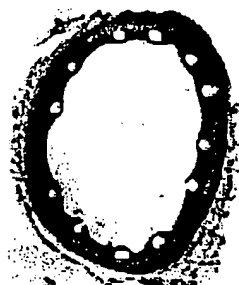
FIGURE 28



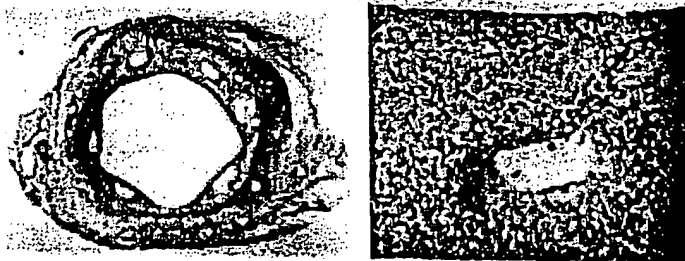
**FIGURE 29**



**FIGURE 30**



**FIGURE 31**



**FIGURE 32**

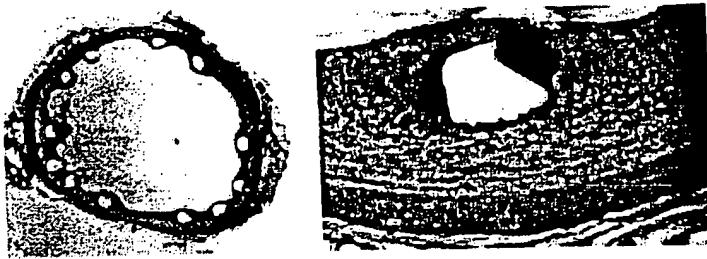


**FIGURE 33**

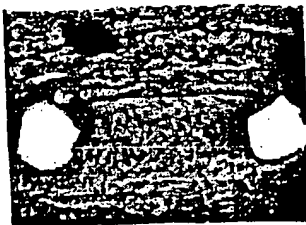


**FIGURE 34**



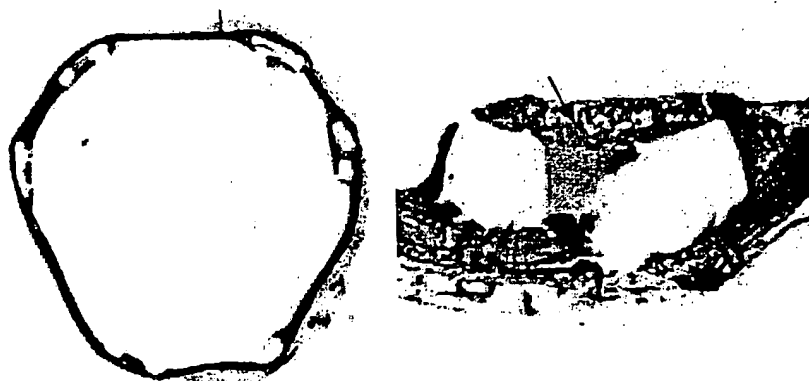


**FIGURE 35**

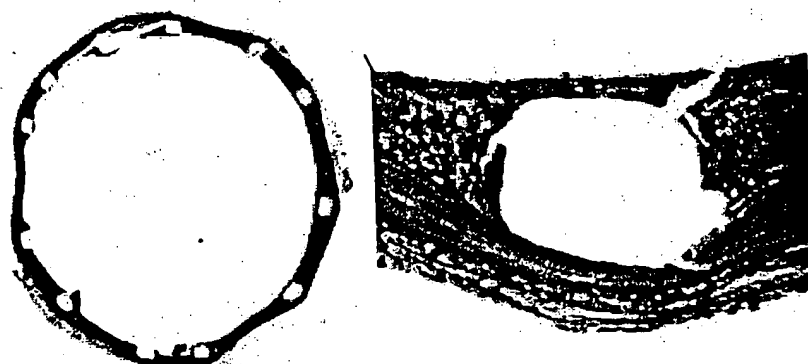


**FIGURE 36**

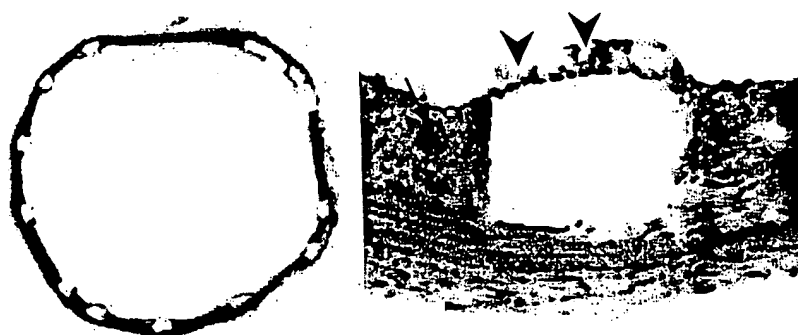
**FIGURE 37**

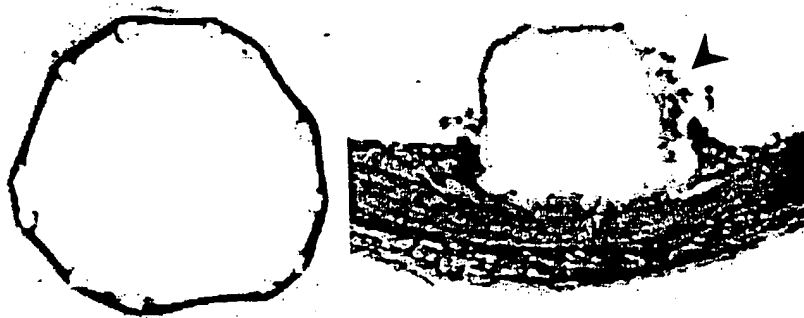


**FIGURE 38**



**FIGURE 39**

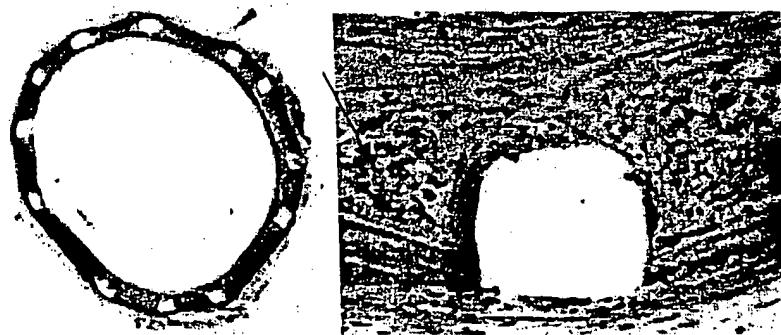




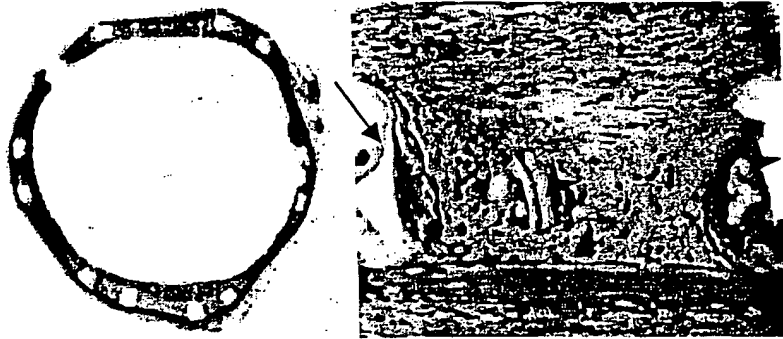
**FIGURE 40**



**FIGURE 41**



**FIGURE 42**



**FIGURE 43**

uncrimped/unexpanded

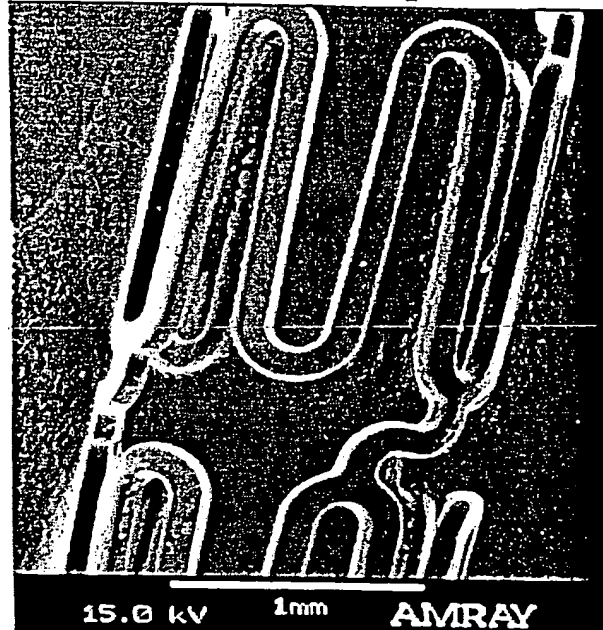


FIG. 44a



FIG. 44b

uncrimped/unexpanded

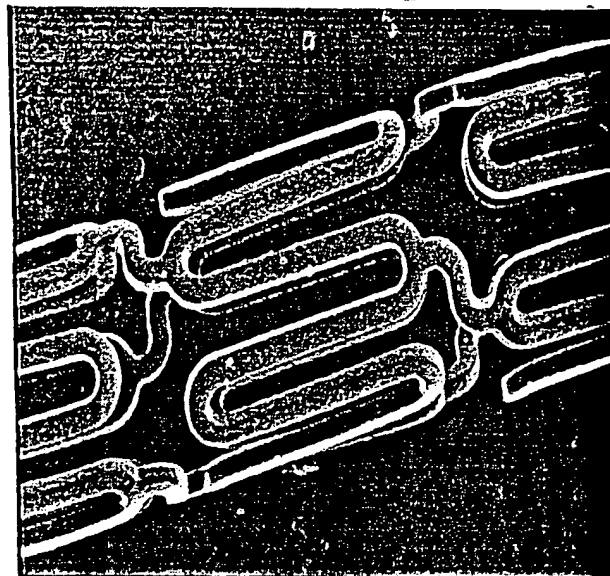


FIG. 45a

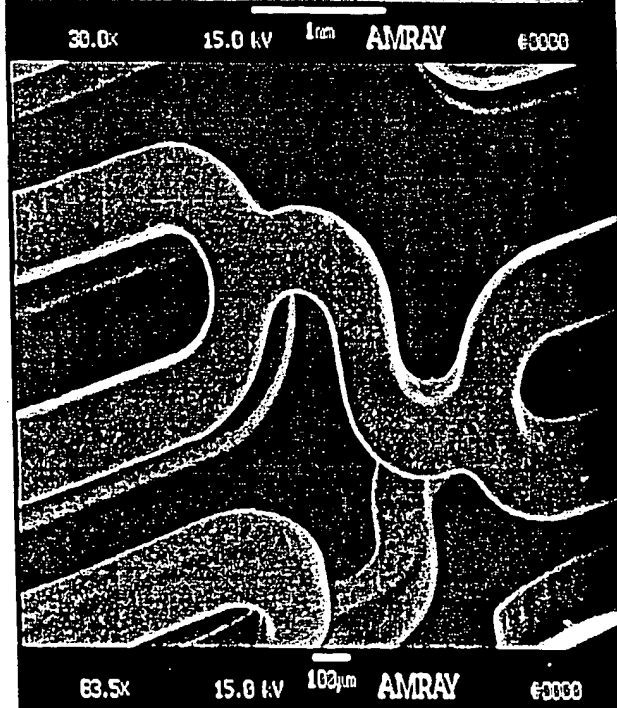


FIG. 45b

uncrimped/unexpanded

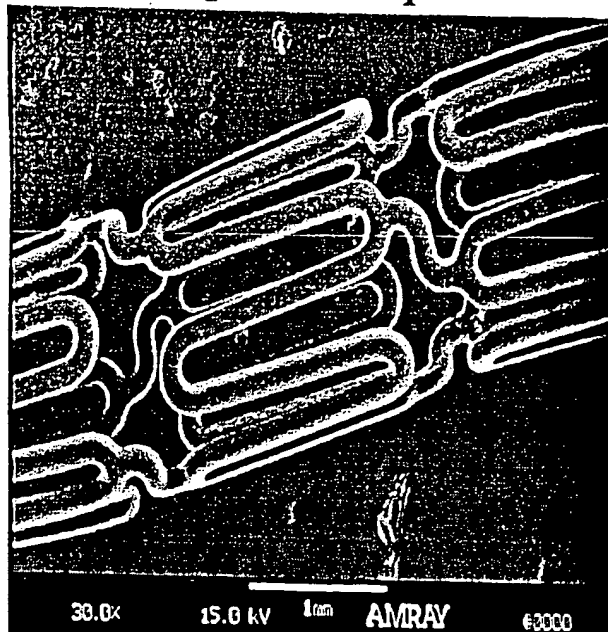


FIG. 46a

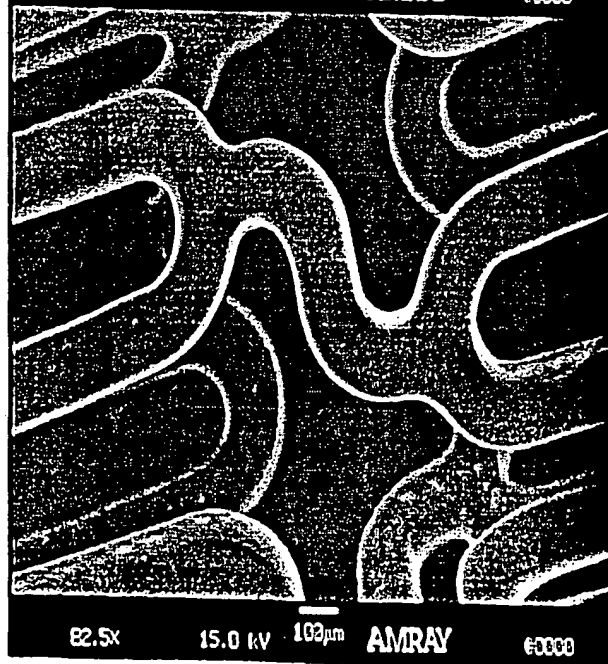
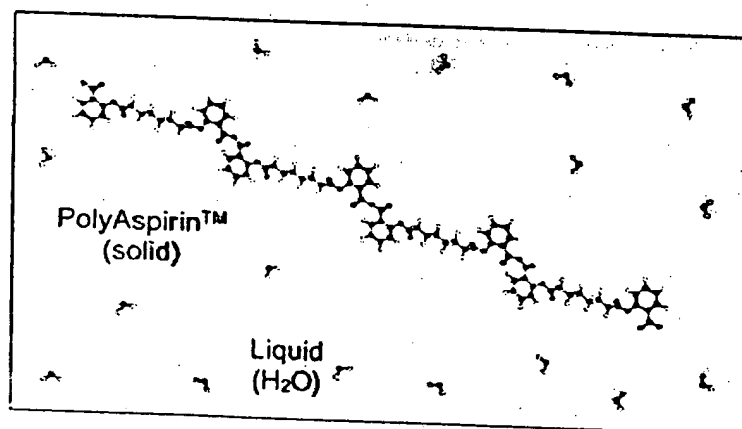


FIG. 46b

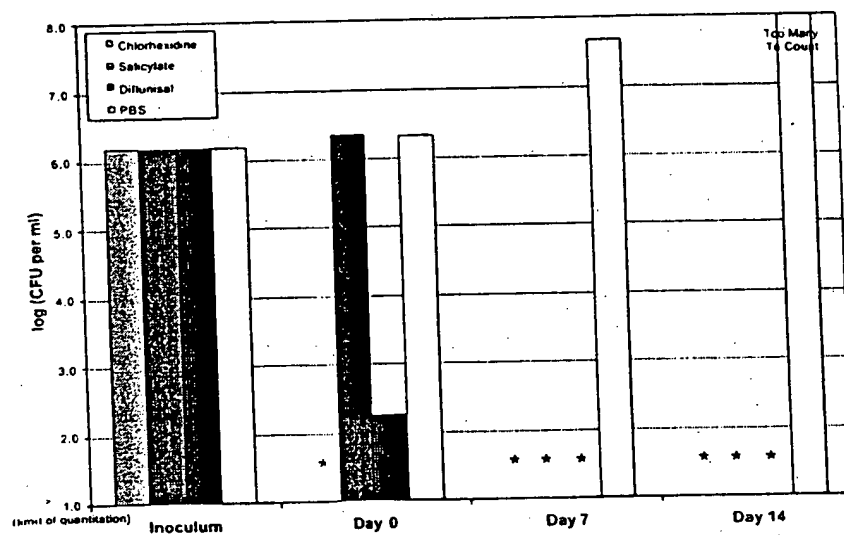


**FIGURE 47**

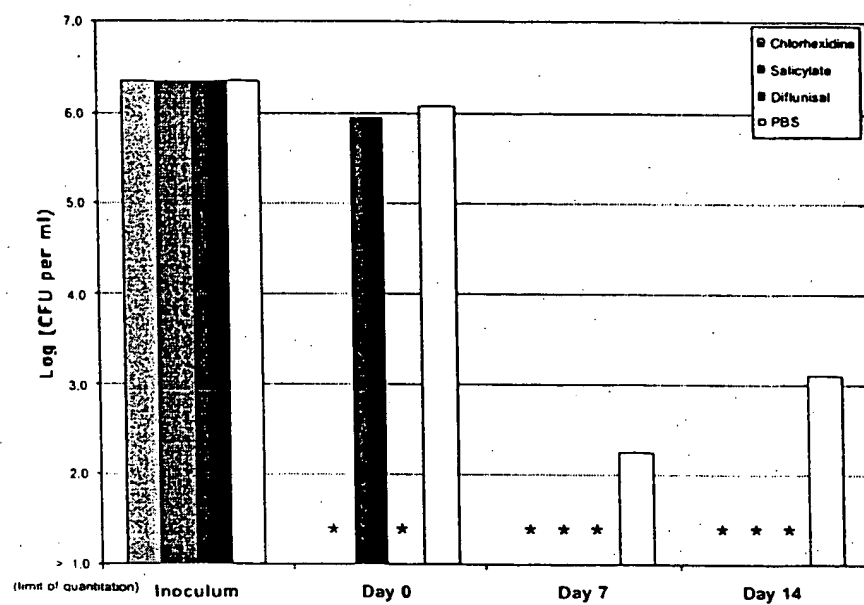




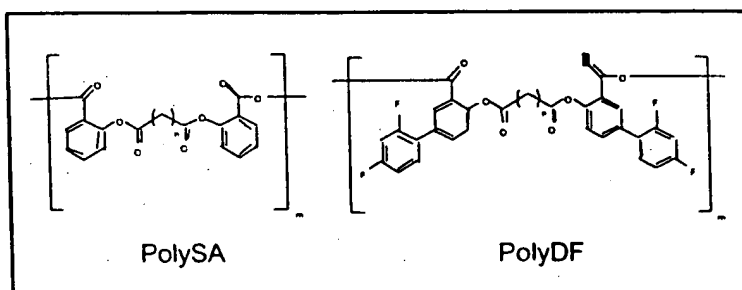
**FIGURE 48**



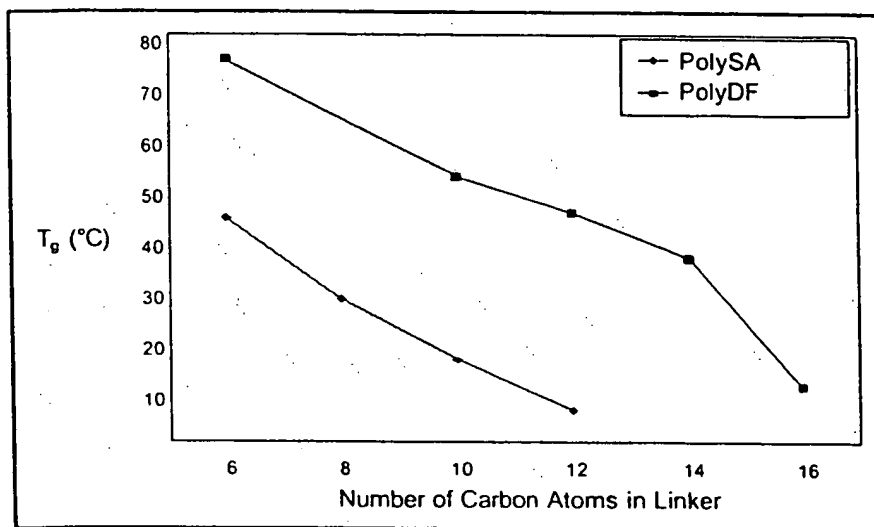
**FIGURE 49**



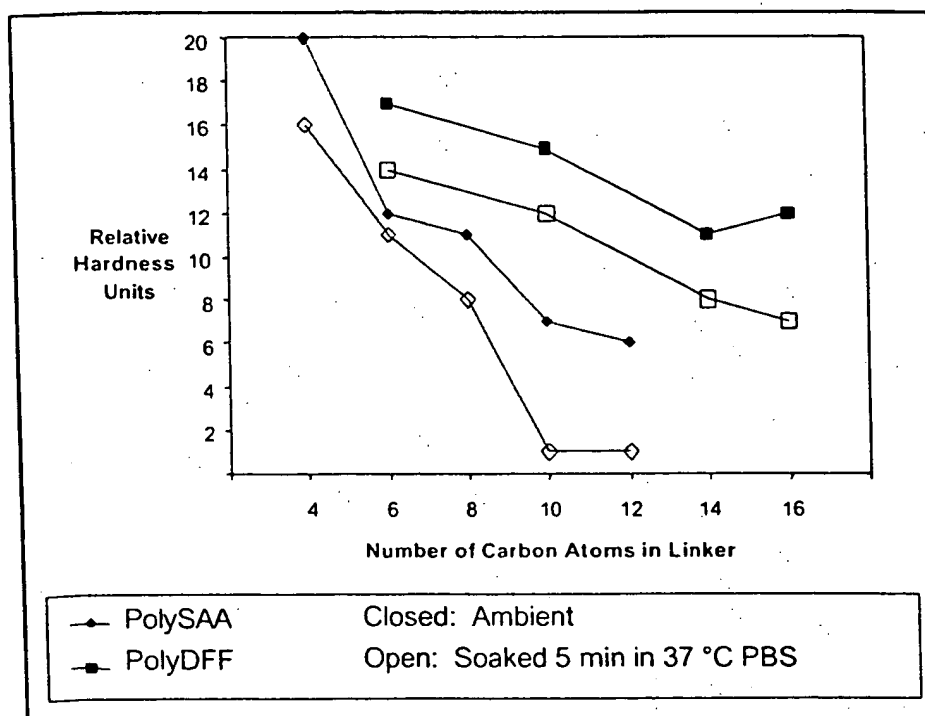
**FIGURE 50**



**FIGURE 51**



**FIGURE 52**



**FIGURE 53**

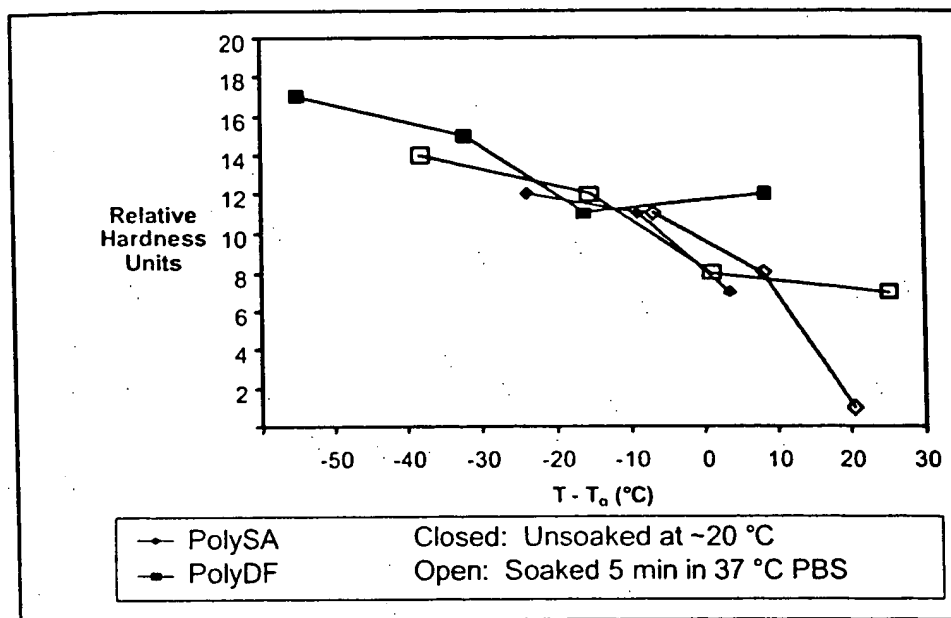
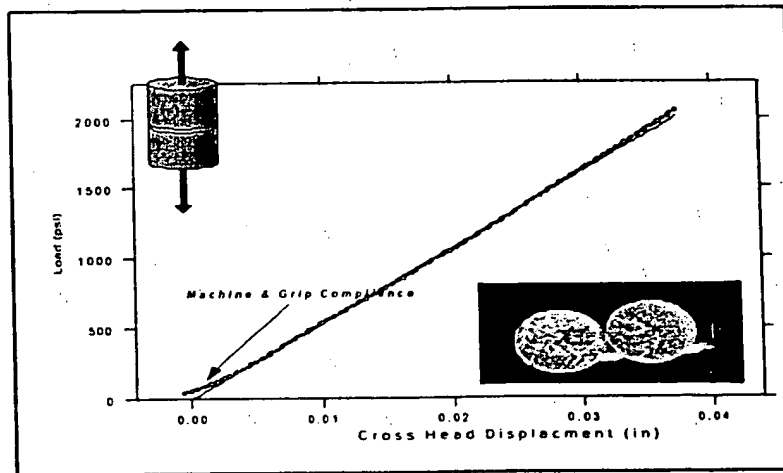
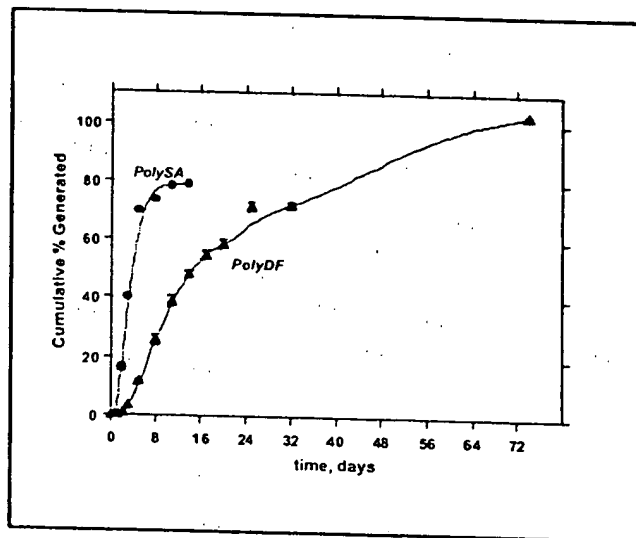


FIGURE 54

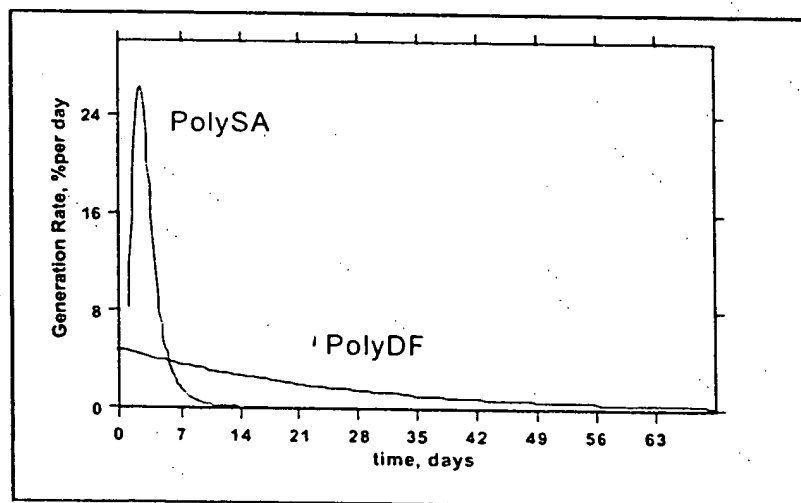


**FIGURE 55**

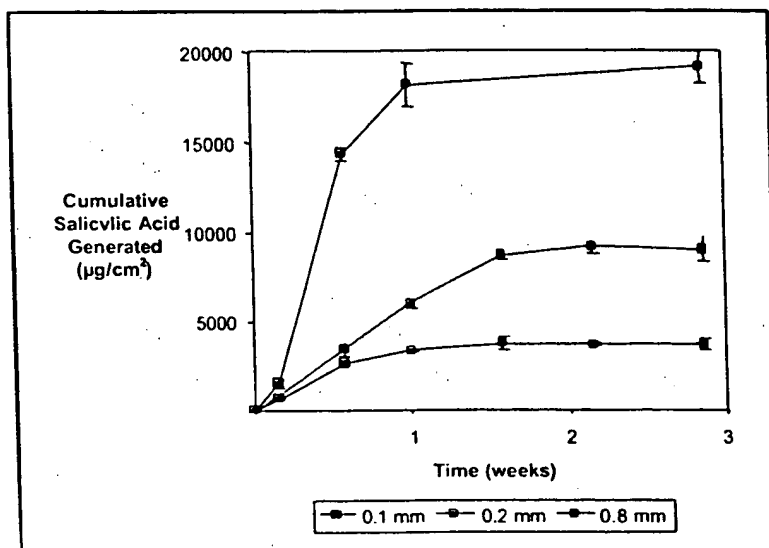




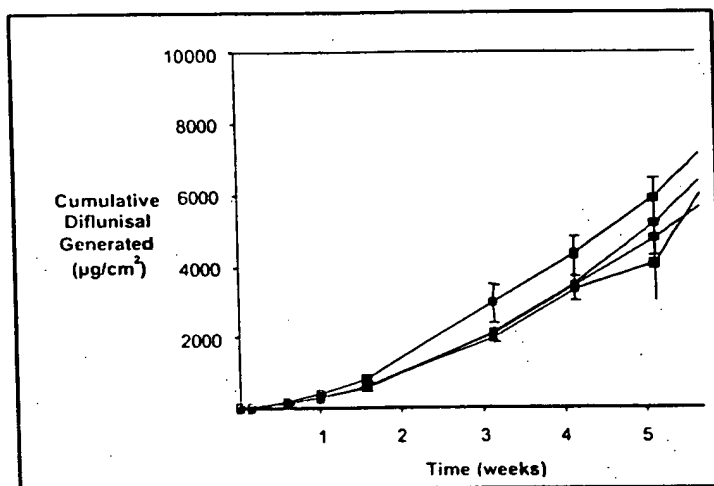
**FIGURE 56**



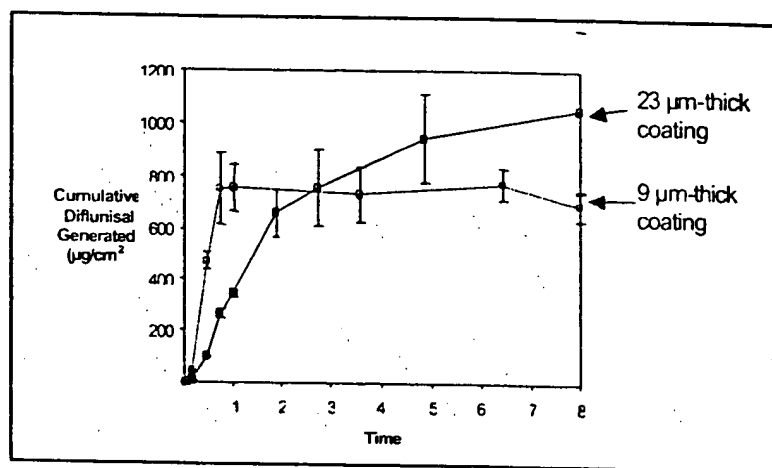
**FIGURE 57**



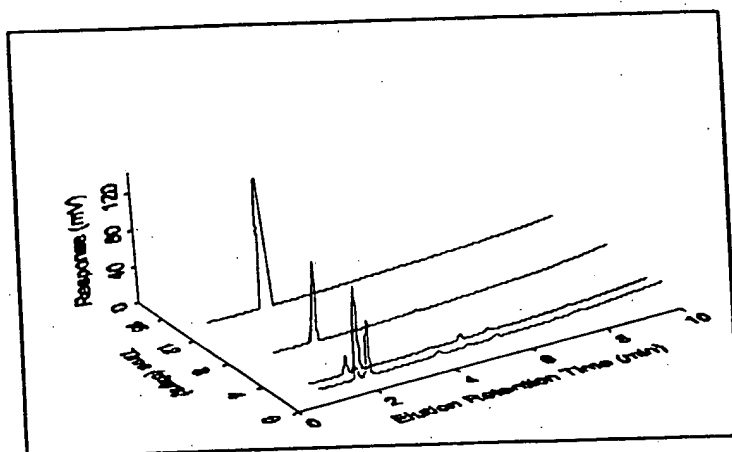
**FIGURE 58**



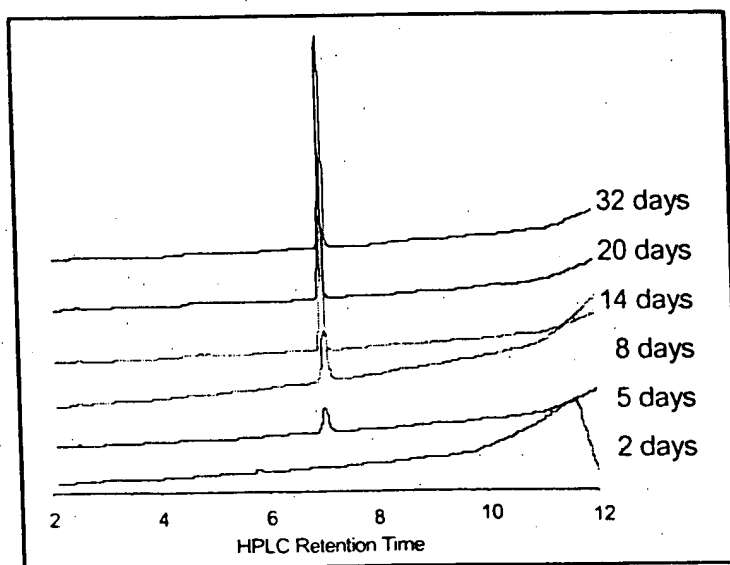
**FIGURE 59**



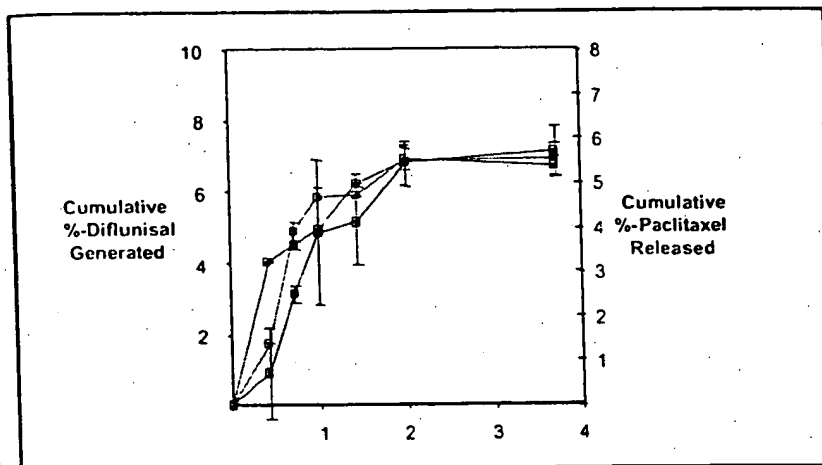
**FIGURE 60**



**FIGURE 61**

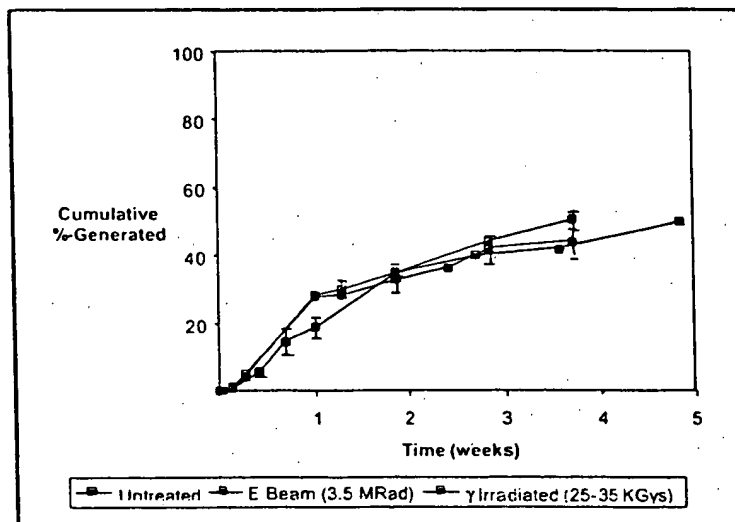


**FIGURE 62**

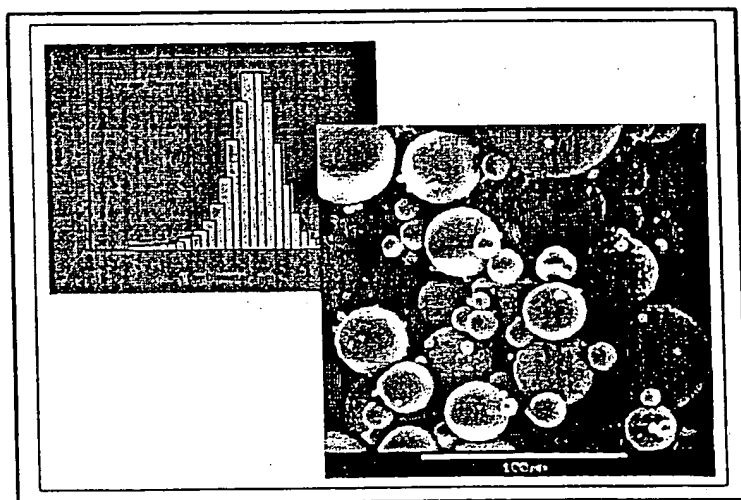


**FIGURE 63**

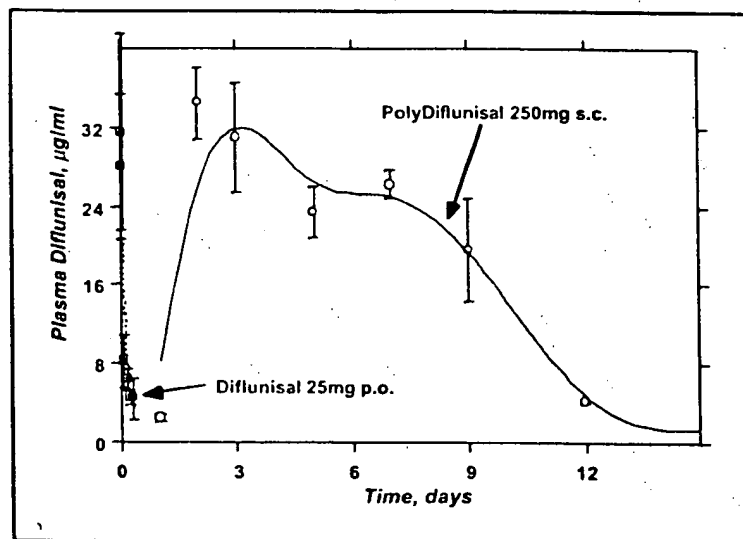




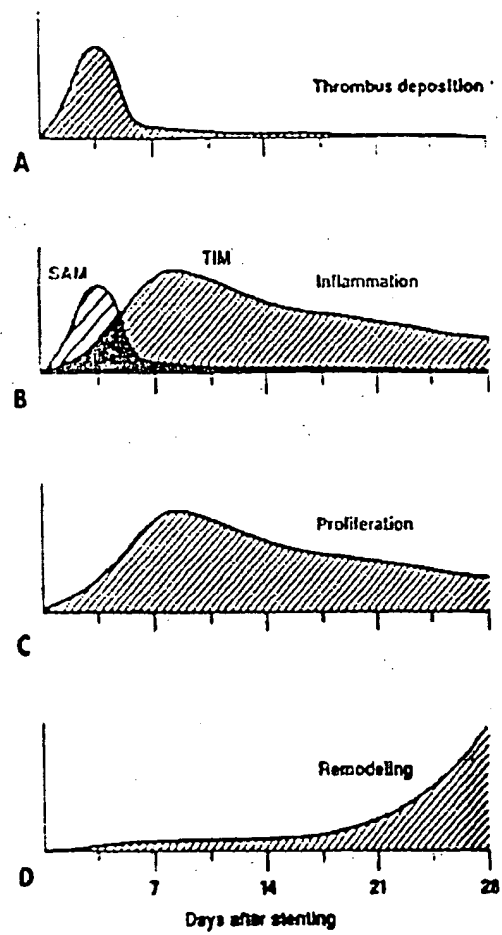
**FIGURE 64**



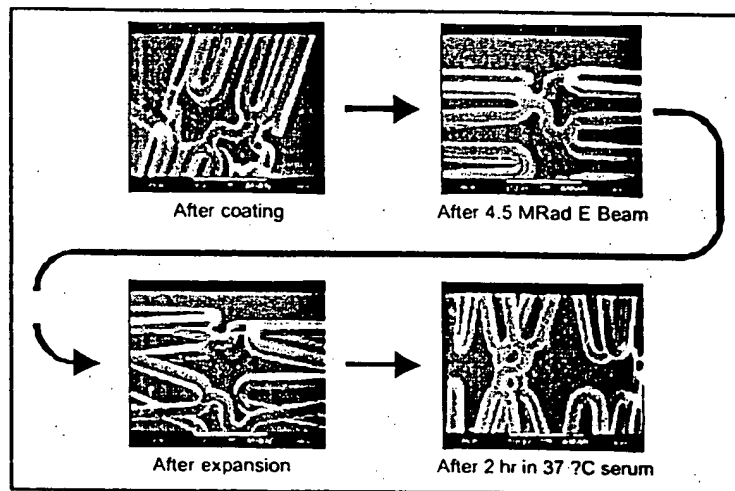
**FIGURE 65**



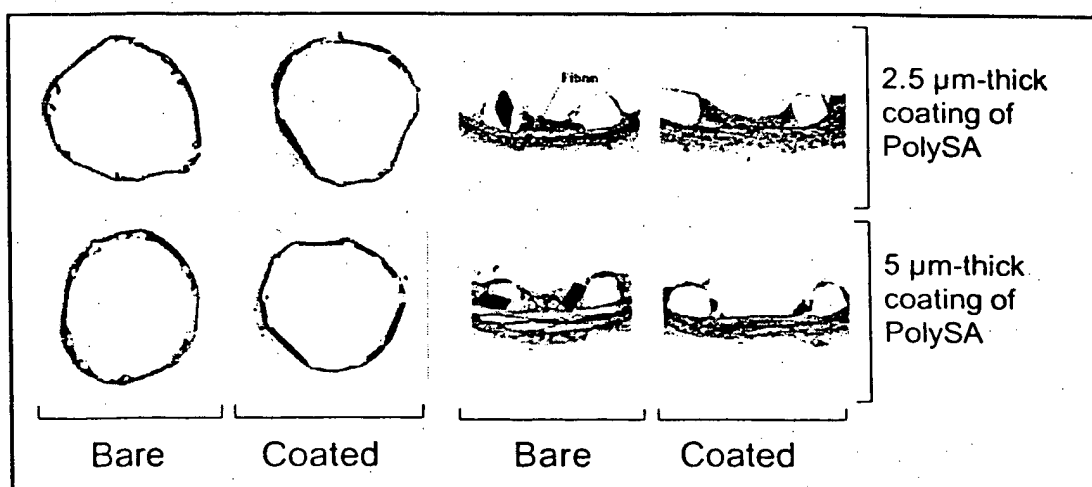
**FIGURE 66**



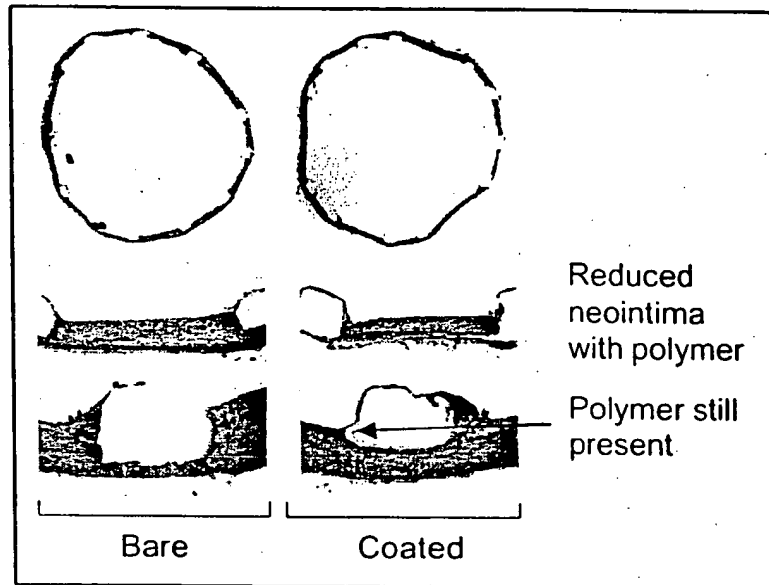
**FIGURE 67**



**FIGURE 68**



**FIGURE 69**



**FIGURE 70**

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